

**FIG.\_ 1****FIG.\_ 1A****FIG.\_ 1B****FIG.\_ 1A****SEQ ID NO: 1****Nucleotide Sequence Tankyrase Homologue isotype1**

CTTTGAAGACACTGGATTCATACTTTGCCTGGGTTATCTCTGTGTCACATAGACAAATA  
TTAGCTGTGAGCAGATCTTTGTTGCTTGTAGTCCCCAGTTAGCAGAAACATTCTGTGAGA  
TAGATGTGGGAAAGGAATTCTAGCAAGAGTTGTCAGTGTATCATAAGGTGTGATTACATATTAA  
GTTTTATACTTTAACATCTGAAAATGTATACTAAATATGCAGAACTCTATTGTAGAGTGAGAAA  
CATTTGAACCTTGAGCTTCAGTCATTATTGTATTCTTCTTGAGGTTAGCAGTAGTACCAACCCA  
AGGCAC TGCTTAGGTACCACTGCTGCTTAGTGGAGAGTCCCTCTGGCTTATCATTAGGTTGGCG  
GAAAGACGTAGTTGAATATTGCTTCAGAATGGTCAAGTGTCCAAGCAGTGATGATGGGGCCTTAT  
TCCTCTCATAATGCATGCTCTTGGTCACTGCTGAAGTAGTCATTCCCTTGCGACATGGTGAGA  
CCCCAATGCTCGAGATAATTGAATTATACTCCTCTCCATGAAGCTGCAATTAAAGGAAAGATTGATGT  
TTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCACCGAAATACAGATGGAAGGACAGCATTGGA  
TTTAGCAGATCCATCTGCCAAAGCAGTGCTACTGGTGAATATAAGAAAGATGAACTCTTAGAAAGTGC  
CAGGAGTGGCAATGAAGAAAAATGATGGCTCTACTCACACCATTAAATGTCAGTGCACGCCAGTGA  
TGGCAGAAAGTCAACTCCATTACATTGGCAGCAGGATATAACAGAGTAAAGATTGTACAGCTGTTACT  
GCAACATGGAGCTGATGTCATGCTAAAGATAAAAGGTGATCTGGTACCATACACAATGCCTGTTCTTA  
TGGTCATTATGAAGTACTGAACTTTGGTCAAGCATGGTGCCTGTGTAATGCAATGGACTGTGGCA  
ATTCACTCCTCTCATGAGGCAGCTCTAAGAACAGGGTTGAAGTATGTTCTCTCTTAAGTTATGG  
TGCAGACCCAACACTGCTCAATTGTCACAATAAAAGTCTAGACTTGGCTCCACACCACAGTTAAA  
AGAAAGATTAGCATATGAATTAAAGGCCACTCGTTGCTGCAAGCTGCACGAGAAGCTGATGTTACTCG  
AATCAAAAAACATCTCTCTGGAAATGGTGAATTCAAGCATCCTCAAACACATGAAACAGCATTGCA  
TTGTGCTGCTGCATCTCCATATCCAAAAGAAAGCAAATATGTGAACTGTTGCTAAGAAAAGGAGCAA  
CATCAATGAAAAGACTAAAGAATTCTTGACTCCTCTGCACGTGGCATCTGAGAAAGCTCATAATGATGT  
TGGTGAAGTAGTGGTGAACATGAAGCAAAGGTTAATGCTCTGGATAATCTGGTCAGACTCTACA

CAGAGCTGCATATTGGTCATCTACAAACCTGCCCTACTCCTGAGCTATGGGTGTGATCCTAACAT  
TATATCCCTCAGGGCTTACTGCTTACAGATGGAAATGAAATGTACAGCAACTCCTCCAAGAGGG  
TATCTCATTAGGTAAATTAGGCAGACAGACAATTGCTGGAAGCTGCAAAGGCTGGAGATGTCGAAAC  
TGTAAAAAAACTGTGTACTGTTAGGTCAACTGCAGAGACATTGAAGGGCGTCAGTCTACACCAACT  
TCATTTGCAGCTGGGTATAACAGAGTGTCCGTGGAAATATGCTACAGCATGGAGCTGATGTGCA  
TGCTAAAGATAAAAGGAGGCCTGTACCTTGACAATGCATGTTATGGACATTATGAAGTTGAGA  
ACTTCTTGTAAACATGGAGCAGTAGTTAATGAGCTGATTATGGAAATTACACCTTACATGAAGC  
AGCAGCAAAAGGAAATATGAAATTGCAAACCTCTGCTCCAGCATGGTGAGACCCCTACCAAAAAAAA  
CAGGGATGGAAATACTCCTTGGATCTGTTAAAGATGGAGATAAGATATTCAAGATCTGCTTAGGGG  
AGATGCGAGCTTGCTAGATGCTGCCAAGAAGGGTGTAGCCAGAGTGAAGAAGTTGCTTCTCCTGA  
TAATGTAATTGCCGCGATACCAAGGCAGACATTCAACACCTTACATTAGCAGCTGGTTATAATAA  
TTTAGAAGTTGCAGAGTATTGTTACAACACGGAGCTGATGTAATGCCAAGACAAAGGAGGACTTAT  
TCCTTACATAATGCAGCATCTACGGGATGAGATGAGCTAGCAGCTCTACTAATAAGTATAATGCATG  
TGTCAATGCCACGGACAAATGGGCTTCACACCTTGACGAAGCAGGCCAAAGGACGAACACAGCT  
TTGTGCTTGCTAGCCATGGAGCTGACCCACTCTAAAATCAGGAAGGACAAACACCTTAGA  
TTTAGTTTCAGCGGATGATGTCAGCGCTCTGACAGCAGCCATGCCCATCTGCTCTCCAGGTCC  
TTACAAGCCTCAAGTGCCTAATGGGTGAGAAGCCCAGGAGCCACTGCAGATGCTCTCTTCAGGTCC  
ATCTAGCCCATCAAGCCTTCTGCAGCCAGCAGTCTGACAACCTATCTGGAGTTTCAGAACTGTC  
TTCAGTAGTTAGTCAGTGGAACAGAGGGTGTCCAGTTGGAGAAAAGGAGGTTCCAGGAGTAGA  
TTTAGCATAACTCAATTGTAAGGAATCTGGACTTGAGCACCTAATGGATATATTGAGAGAGAAC  
GATCACTTGGATGTATTAGTTGAGATGGGCACAAGGAGCTGAAGGAGATTGGAATCAATGCTTATGG  
ACATAGGCACAAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAACAAGGTCTAACCCATATT  
AACTTGAACACCTCTGGTAGTGGAACAAATTCTTATAGATCTGCTCTGATGATAAGAGTTCACTG  
TGTGGAGGAAGAGATGCAAAGTACAGTTCGAGAGCACAGAGATGGAGGTCTGCAGGTGGAAATCTCAA  
CAGATACAATATTCTCAAGATTAGGTTGTAACAAGAAACTATGGAAAGATAACACTCACCGGAG  
AAAAGAAGTTCTGAAGAAAACCACAACCATGCCATGAACGAATGCTATTCTGAGGTCTCCTTTGT  
GAATGCAATTATCCACAAAGGCTTGATGAAAGGCATGCGTACATAGGTGGTATTTGGAGCTGGCAT  
TTATTTGCTGAAAACCTCTCCAAAAGCAATCAATATGTATATGGAATTGGAGGAGGTACTGGGTGTCC  
AGTTCACAAAGACAGATCTGTTACATTGCCACAGGCAGCTGCTCTTGCCGGTAACCTGGAAA  
GTCTTCTGCAAGTTCAGTGCAATGAAAATGGCACATTCTCCTCCAGGTCTACACTCAGTCAGTGGTAG  
GCCAGTGTAAATGGCCTAGCATTAGCTGAATATGTTATTACAGAGGAGAACAGGCTTACCTGAGTA  
TTAATTACTTACCAAGATTAGGGCCTGAAGGTATGGTGTGATGGATAAATAGTTATTAAAGAAACTA  
ATTCCACTGAACCTAAAATCATCAAAGCAGCAGTGGCCTCTACGTTTACTCCTTGCTGAAAAAAA  
AA

**FIG.-1B**

**FIG.\_2****FIG.\_2A****FIG.\_2B****FIG.\_2A****SEQ ID NO: 2****Nucleotide Sequence Tankyrase Homologue isotype2**

CGCGCTGCTCCGCCCGCCGGGGCAGCCGGGGCAGGGAGCCCAGCGAGGGCGCGTGGCGCG  
CCCAGGGACTGCCGGATCCGGTACAGCAGGGAGCCAAGCGGCCGGCCCTGAGCGCGTCTCTC  
CGGGGGGCCCTGCCCTCCTGCTCGCGGGCCGGCTCCTGCTCCGGTTGCTGGCGCTGTTGCTGGCTG  
TGGCGGGCGGCCAGGATCATGTCGGGTCGCCGCTGCCGCGGGGAGCGGCCCTGCCGAGCGGCCGCG  
CCGAGGCCGTGGAGCCGGCCCGAGAGCTGTTGAGGCCTGCCGCAACGGGACGTGGAACGAGTCA  
AGAGGCTGGTACGCCCTGAGAAGGTGAACAGCCGACACGGCGGGCAGGAAATCCACCCGCTGCAC  
TCGCCGCAGGTTTGGCGAAAGACGTAGTTGAATATTGCTTCAGAATGGTCAAATGTCCAAGCAC  
GTGATGATGGGGCCCTTATTCCCTTCATAATGCATGCTCTTGGTATGCTGAAGTAGTCAATCTCC  
TTTGCACATGGTGCAGACCCAAATGCTCGAGATAATTGGAATTATACTCCTCTCCATGAAGCTGCAA  
TTAAAGGAAAGATTGATGTTGCATTGTGCTGTTACAGCATGGAGCTGAGCCAACCATCGAAATACAG  
ATGGAAGGACAGCATTGGATTAGCAGATCCATGCCAAAGCAGTGCTTACTGGTGAATATAAGAAAG  
ATGAACCTTAGAAAGTGCAGGAGTGGCAATGAAGAAAAATGATGGCTACTCACACCATAATG  
TCAACTGCCACGCAAGTGAATGGCAGAAAGTCAACTCCATTACATTGGCAGCAGGATATAACAGAGTAA  
AGATTGTACAGCTGTTACTGCAACATGGAGCTGATGTCCATGCTAAAGATAAAGGTGATCTGGTACCAT  
TACACAATGCCCTGTTCTTATGGTCAATTGAAAGTAACTGAACCTTGGTCAAGCATGGCCTGTGAA  
ATGCAATGGACTTGTGGCAATTCACTCCCTTCATGAGGCAGCTCTAAGAACAGGGTTGAAGTATGTT  
CTCTCTCTTAAGTTATGGTGCAGACCCAAACACTGCTCAATTGTCACAATAAAAGTGTATAGACTTGG  
CTCCCACACCACAGTTAAAGAAAGATTAGCATATGAATTAAAGGCCACTCGTTGCTGCAAGCTGCAC  
GAGAAGCTGATGTTACTCGAATCAAAAACATCTCTGAAATGGTGAATTCAAGCATCCTCAA  
CACATGAAACAGCATTGCATTGTGCTGCACTCCATATCCAAAAGAAAGCAAATATGTGAAGTGT  
TGCTAAGAAAAGGAGCAAACATCAATGAAAAGACTAAAGAATTCTGACTCCTCTGCACGTGGCATCTG  
AGAAAGCTCATAATGATGTTGAAGTAGTGGTAAACATGAAGCAAAGTTAATGCTCTGGATAATC

TTGGTCAGACTCTACACAGAGCTGCATATTGGTCATCTACAAACCTGCCGCTACTCCTGAGCT  
ATGGGTGTGATCTAACATTATATCCCTCAGGGTTACTGCTTACAGATGGAAATGAAAATGTAC  
AGCAACTCCTCCAAGAGGGTATCTCATTAGGTAAATTAGGAGCAGACAGACAATTGCTGGAAGCTGCAA  
AGGCTGGAGATGTCGAAACTGTAAAAAAACTGTGTACTGTTCAGAGTGTCAACTGCAGAGACATTGAAG  
GGCGTCAGTCTACACCACTTCATTGAGCTGGTATAACAGAGTGTCCGTGGTGAATATCTGCTAC  
AGCATGGAGCTGATGTGCATGCTAAAGATAAAGGAGGCCCTGTACCTTGACAAATGCATGTTCTTATG  
GACATTATGAAGTTGAGAACTTCTGTTAACATGGAGCAGTAGTTAATGTAGCTGATTATGGAAAT  
TTACACCTTACATGAAGCAGCAGCAAAGGAAATATGAAATTGCAAACCTCTGCTCCAGCATGGTG  
CAGACCCTACCAAAAAACAGGGATGGAATACTCCTTGGATCTGTTAAAGATGGAGATAACAGATA  
TTCAAGATCTGCTTAGGGAGATGCAGCTTGCTAGATGCTGCCAAGAAGGGTTGTTAGCCAGAGTGA  
AGAAGTTGCTTCTGATAATGTAATTGCCGCGATAACCAAGGCAGACATTCAACACACCTTACATT  
TAGCAGCTGGTTATAATAATTAGAAGTTGAGAGTATTGTTACAACACGGAGCTGATGTGAATGCC  
AAGACAAAGGAGGACTTATTCTTACATAATGCAGCATCTACGGGATGTAGATGTAGCAGCTCTAC  
TAATAAAAGTATAATGCATGTCATGCCACGGACAAATGGCTTACACCTTGACGAAGCAGGCC  
AAAAGGGACGAACACAGCTTGTGCTTGTCTAGCCATGGAGCTGACCGACTCTAAAAATCAGG  
AAGGACAAACACCTTAGATTTAGTTAGCTCAGCGGATGATGTCAGCGCTCTGACAGCAGCCATGCC  
CATCTGCTCTGCCCTTTGTTACAAGCCTCAAGTGTCAATGGGTGAGAAGCCCAGGAGCCACTGCAG  
ATGCTCTCTCTTCAGGTCCATCTAGCCATCAAGCCTTCTGCAGCCAGCAGTCTGACAACATTCTG  
GGAGTTTCAGAACTGCTTCAGTAGTTCAAGTGGAACAGAGGGTGTCCAGTTGGAGAAAA  
AGGAGGTTCCAGGAGTAGATTTAGCATAACTCAATTGTAAGGAATCTGGACTTGAGCACCTAATGG  
ATATATTGAGAGAGAACAGATCACTTGGATGTATTAGTTGAGATGGGCACAAGGAGCTGAAGGAGA  
TTGGAATCAATGCTTATGGACATAGGCACAAACTAATTAAAGGAGTCGAGAGACTTATCTCCGGACAAC  
AAGGTCTAACCCATATTAACTTGAACACCTCTGGTAGTGGAACAAATTCTTATAGATCTGCTCTG  
ATGATAAAAGAGTTCAGTCTGTGGAGGAAGAGATGCAAAGTACAGTTCAGAGCAGAGATGGAGGTC  
ATGCAGGTGGAATCTCAACAGATAAAATTCTCAAGATTCAAGAGTTGTAACAAGAAACTATGGG  
AAAGATAACACTACCGGAGAAAAGAAGTTCTGAAGAAAACCACAACCAGCCAATGAACGAATGCTAT  
TTCATGGGTCTCTTGTGAATGCAATTATCCACAAAGGCTTGTGAAAGGCATGCGTACATAGGTG  
GTATGTTGGAGCTGGCATTATTGCTGAAAAGTCTCCAAAAGCAATCAATATGTATATGGAATTG  
GAGGAGGTACTGGGTGTCCAGTTCAAAAGACAGATCTGTTACATTGCCACAGGCAGCTGCTCTT  
GCCGGGTAACCTGGAAAGTCTTCCTGCAGTTCAAGTGAATGAAAATGGCACATTCTCCAGGTC  
ATCACTCAGTCAGTGGTAGGCCAGTGTAAATGCCCTAGCATTAGCTGAATATGTTATTACAGAGGAG  
AACAGGCTTATCCTGAGTATTAAATTACCAAGATTGAGGCCTGAAGGTATGGTCATGGATAAA  
TAGTTATTTAAGAAACTAATTCAACTGAACCTAAATCATCAAAGCAGCAGTGGCCTTACGTTTAC  
TCCTTGCTGAAAAAA

**FIG.\_2B**

**SEQ ID NO: 3**

**Amino Acid Sequence Tankyrase Homologue isotype1**

GFGRKDVVEYLLQNGASVQARDDGGIPLHNACSGHAEVNLLRHGADPNARDNWNYTPLHEAAIKG  
KIDVCIVLQLQHGAEPTIRNTDGRITALDADPSAKAVLTGEYKKDELLESARSGNEEK**M**ALLTPLNVNC  
HASDGRKSTPLHLAAGYNRVKIVQLLQHGADVHAKDKGDLVPLHNACSYGHYEVTELLVKHGACVNAM  
DLWQFTPLHEAASKRVECSLLSYGADPTILLNCHNKSAILAPTPQLKERLAYEFKGHSLLQAAREA  
DVTRIKKHLSEMVNFKHPQTHETALHCAAASPYPKRKQICELLRKGANINEKTKEFLTPLHVASEKA  
HNDVVEVVVKHEAKVNALDNLGQTSLHRAAYCGLQTCRLLSYGCDPNIISLQGFTALQMGNENVQQL  
LQEGISLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQHG  
ADVHAKDKGGLVPLHNACSYGHYEVAAELLVKHGAVVNADLWKFPLHEAAAKGKYEICKLLLQHGADP  
TKKNRDGNTPLDLVKDGTDIQDLLRGDAALLDAAKGCLARVKKLSSPDNVNCRDTQGRHSTPLHLAA  
GYNNEVAEYLLQHGADVNAQDKGGIPLHNAASYGHVDVAALLIKYNACVNATDKWAFTPLHEAAQKG  
RTQLCALLLAHGADPTLKNQEGQTPLDLVSADDVSALLTAAMPPSALPSCYKPQVNLNGVRSPGATADAL  
SSGPSSPSSLSAASSLDNLGSFSELSSVSSSGTEGASSLÉKKEVPGVDFSITQFVRNLGLEHLMDF  
EREQITLDVLVEMGHKELKEIGINAYGHRHKLIKGVVERLISGQQGLNPYLTNNTSGSGTILIDLSPDDK  
EFQSVEEMQSTVREHRDGGHAGGI FNRYNILKIQKVCNKLWERYTHRRKEVSEENHNHANERMLFHG  
SPFVNAAIHKGFDERHAYIGGMFGAGIYFAENSSKSQNQVYVGIGGGTGCPVKDRSCYICHRLQLLFCRV  
TLGKSFLQFSAMKMAHSPPGHHSVTGRPSV

**FIG.\_3**

**SEQ ID NO: 4**

**Amino Acid Sequence Tankyrase Homologue isotype2**

RCSARRGAAGGQGAQRGARVGAAGTAPDPVTAGSQAARALSASSPGLALLLAGPGLLLRLALLAV  
AAARIMSGRRCAGGAACASAAAEEAVEPAARELFEACRNGDVERVKRLVTPEKVNSRDTAGRKSTPLHF  
AAGFGRKDVEYLLQNGANVQARDDGGLIPLHNACSFHAEVVNLLLHGADPNARDNWNYTPLHEAAI  
KGKIDVCIVLQLQHGAEPTIRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMALLTPLNV  
NCHASDGRKSTPLHLAAGYNRVKIVQLLLQHGADVHAKDKGDLVPLHNACSYGHYEVTELLVKHGACVN  
AMDLWQFTPPLHEAASKNRVECSLLSYGADPTLLNCHNKSADILAPTPQLKERLAYEFKGHSLLQAAR  
EADVTRIKKHLSEMVNFKHPQTHETALHCAAASPYPKRKQICELLRLKGANINEKTKEFLTPLHVASE  
KAHNDVVEVVVKHEAKVNALDNLGQTSIHRAAYCGHLQTCRLLSYGCDPNIISLQGFTALQMGNENVQ  
QLLQEGLSLGNSEADRQLLEAAKAGDVETVKKLCTVQSVNCRDIEGRQSTPLHFAAGYNRVSVVEYLLQ  
HGADVHAKDKGGLVPLHNACSYGHYEVAEELLVKHGAVVNADLWKFTPLHEAAAKGKYEICKLLLQHGA  
DPTKKNRDGNTPLDLVKDGTDIQDILLRGDAALLDAAKKGCLARVKKLSSPDNVNCRTQGRHSTPLHL  
AAGYNNLEVAEYLLQHGADVNAQDKGGLIPLHNAAASYGHVDVAALLIKYNACVNATDKWAFTPPLHEAAQ  
KGRTQLCALLLAHGADPTLKNQEGQTPLDLSADDVSALLTAAMPPSALPSCYKPQVLNGVRSPGATAD  
ALSSGPSSPSSLSAASSLDNLGSFSSELSSVSSSGTEGASSLEKKEVPGVDFSITQFVRNLGLEHLM  
IFEREQITLDVLVEMGHKELKEIGINAYGHRHKLIKGVVERLISGQQGLNPYLTNTSGSGTILIDLSPD  
DKEFQSVEEEMQSTVREHRDGGHAGGIFNRYNLIKQKVCNKLWERYTHRRKEVSEENHNHANERMLF  
HGSPFVNAAIHKGFDERHAYIGGMFGAGIYFAENSSKSNQYVYGGGTGCPVHKDRSCYICHQOLLFC  
RVTLGKSFLQFSAMKMAHSPPGHHSVTGRPSVNGLALAELYRGEQAYPEYLITYQIMRPEGMVDG

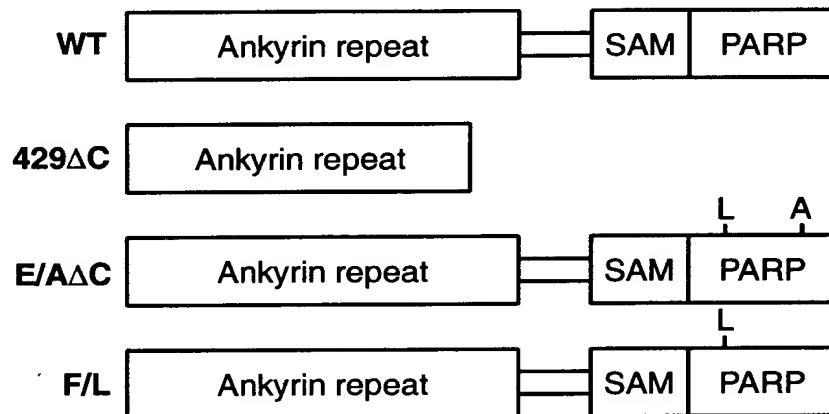
**FIG.\_4**

### Schematic Presentation of Dominant Negative Mutants for Tankyrase Homologue

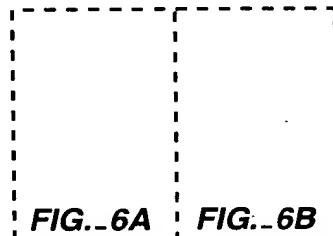
#### Dominant Negative Mutants

Truncation: 429ΔC- of the C-terminal catalytic domain – truncation of the catalytic domain of PARP acts as a dominant negative when overexpressed *in vivo* (Oncogene 1999 Nov 25; 18(50):7010-5)

Point mutant: E945AΔC- conserved residue in PARP domain, thought to be important in NAD<sup>+</sup> binding

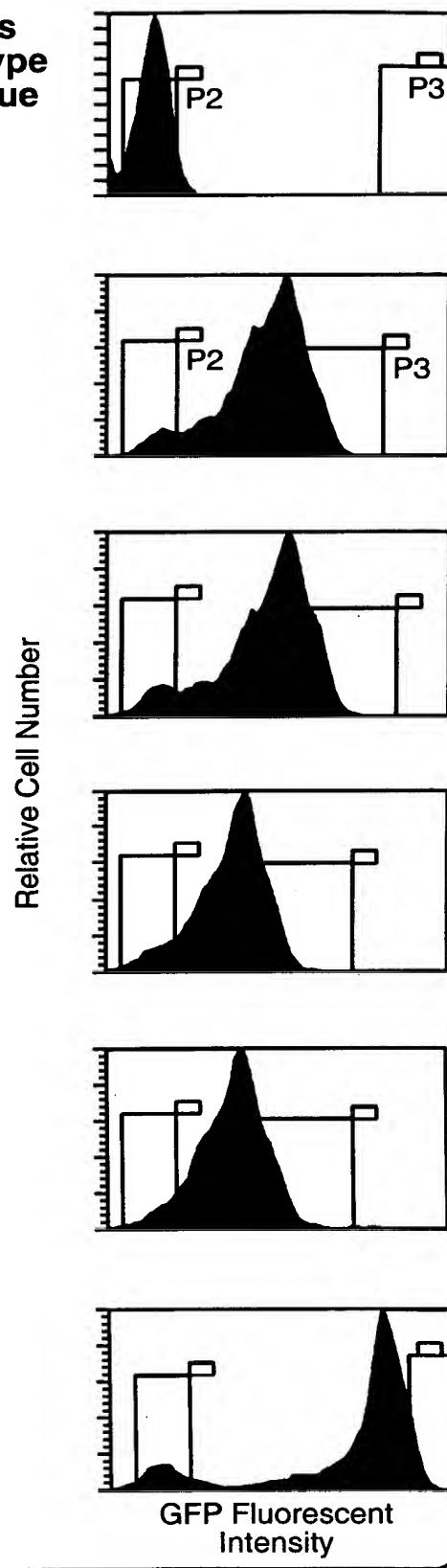


**FIG.\_5**



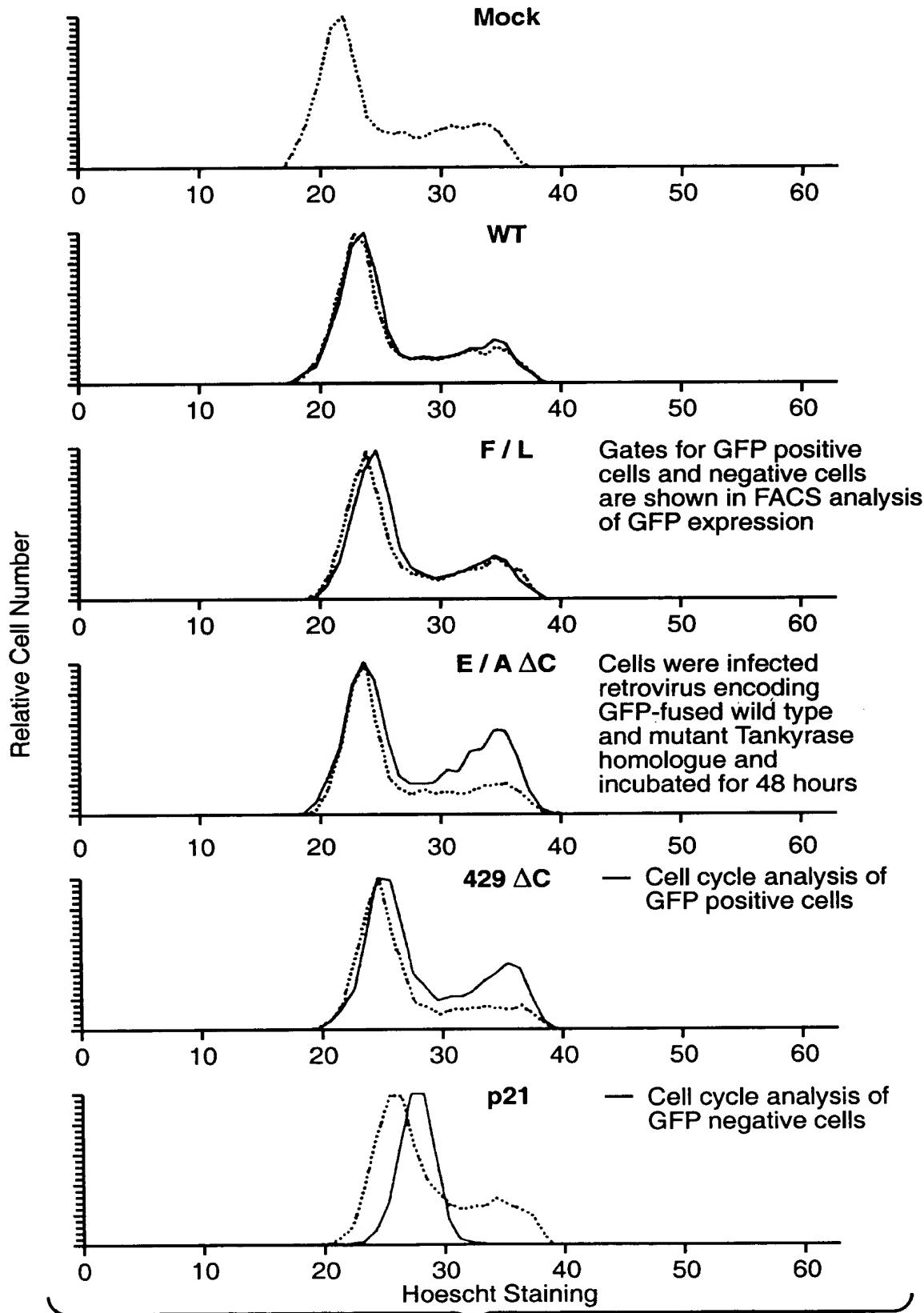
**FIG.\_6**

**Cell Cycle Analysis of A549 Cells  
Infected With GFP-fused Wild Type  
and Mutant Tankyrase Homologue**



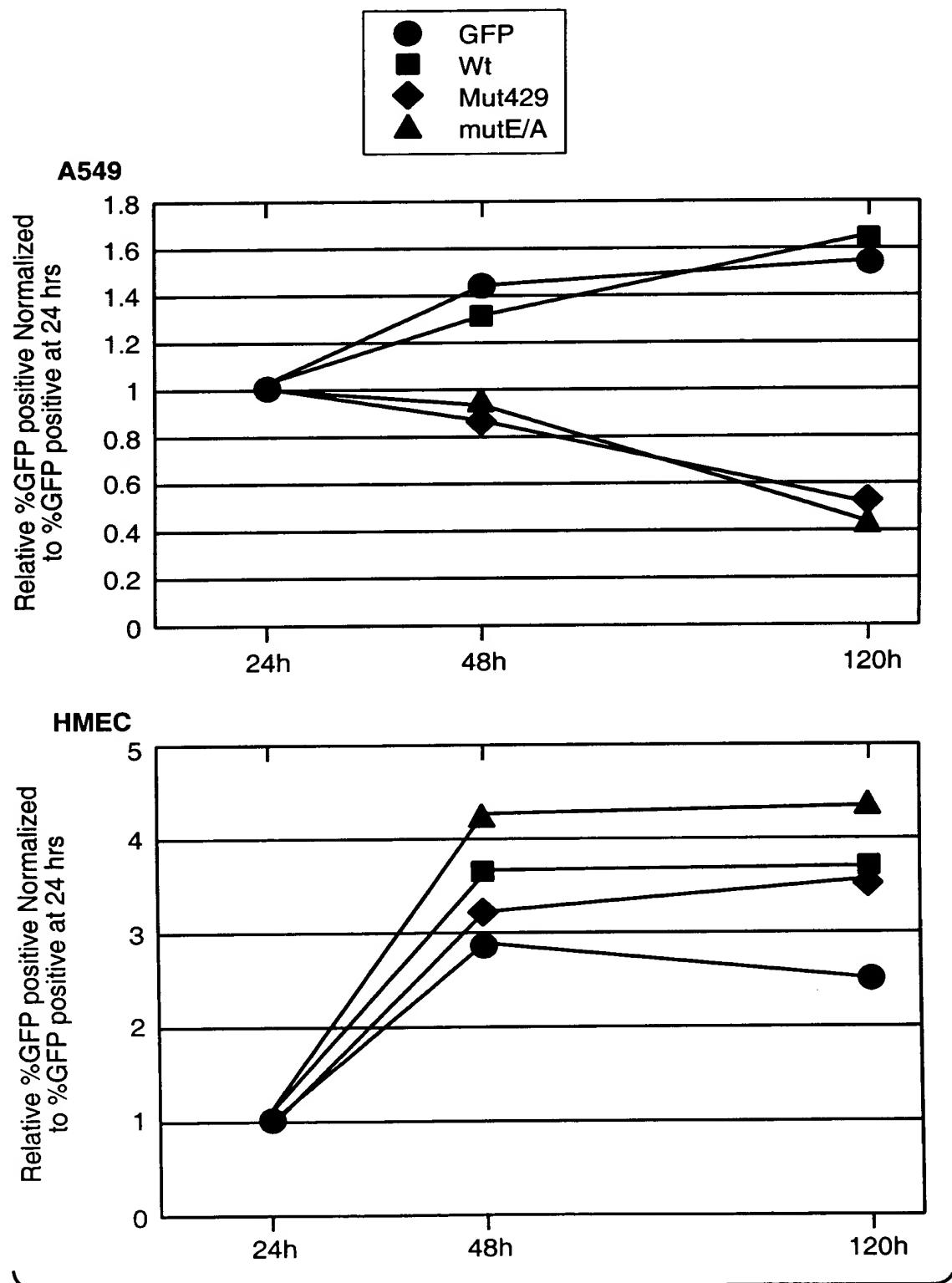
**FIG.\_6A**

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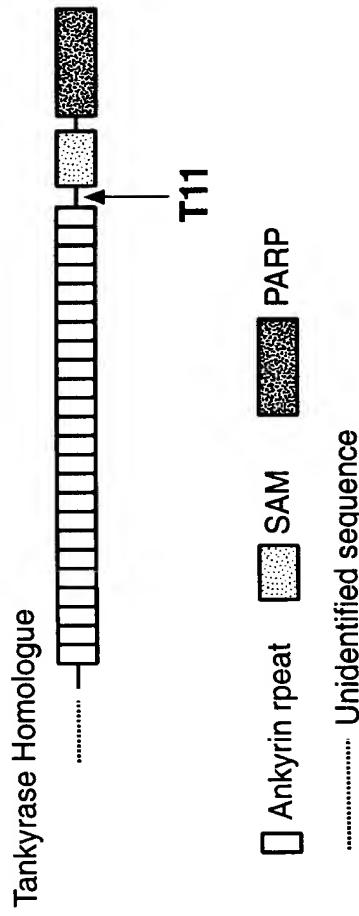
## **FIG.\_6B**

**Kinetics of GFP Positive cells in A549 Cells and Human Mammary Epithelial Cells (HMEC) After Retrovirus Infection Encoding GFP-fused Wild Type and Mutant Tankyrase Homologue**



**FIG.\_7**

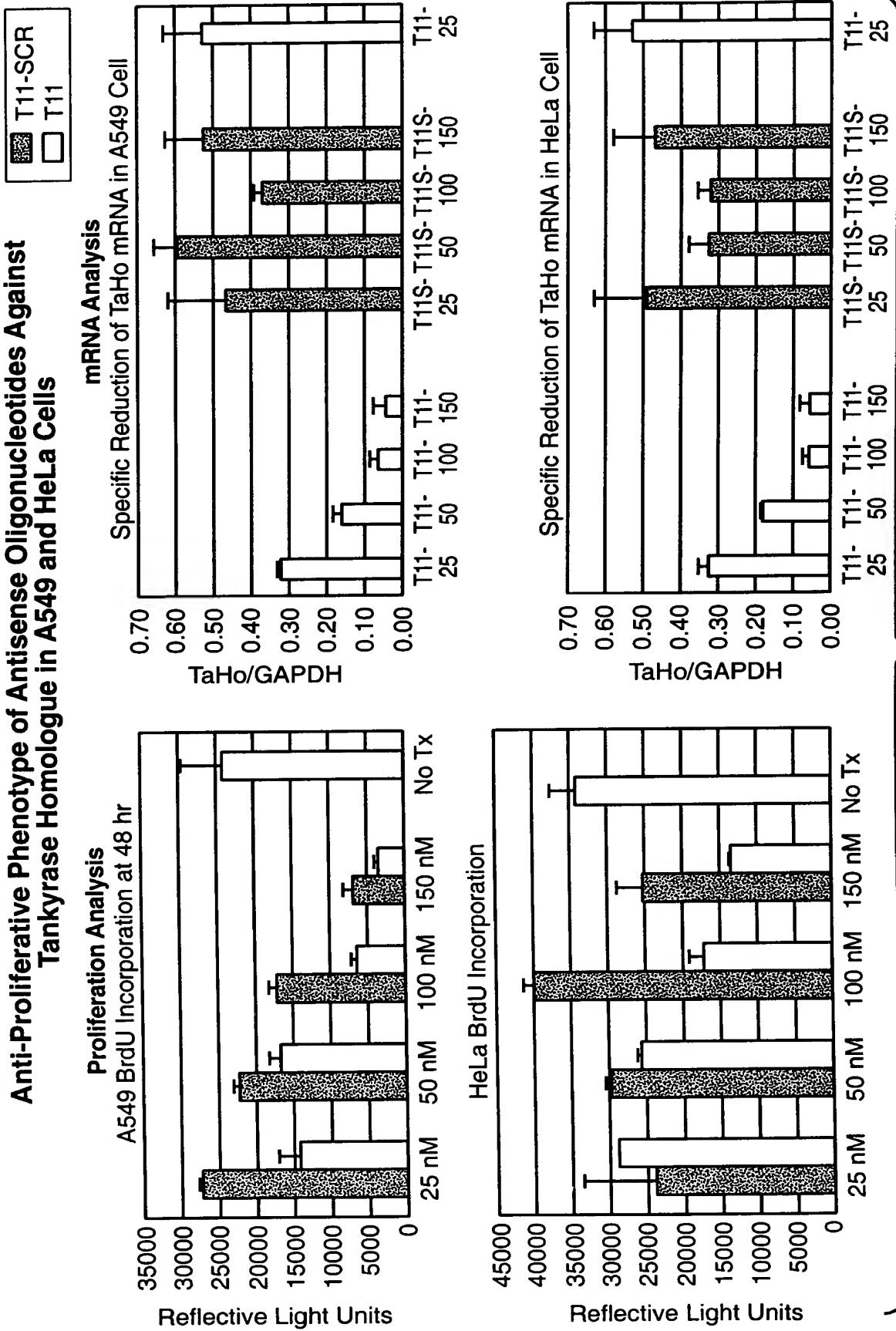
## The Binding Site of Antisense Oligos Against Tankyrase Homologue



T11	Tankyrase	Homologue	Tankyrase	Tankyrase
	GTGGAACAGAGGGTGCCTCC			
	GTGGAACAGAGGGTGCCTCCAGTTGGAGAAAAGGAGGGTTCCAGGAGTAGATTAGCAT			2838
	ATGCAGGGATGGGCCGGGAACAGAAAGGAAGGGAAAGGAAAGTGGCTGGTCAT			3091
	*** * *** * *** * *** *		*** * *** * *** *	*** * *** * *** *

FIG. 8

**Anti-Proliferative Phenotype of Antisense Oligonucleotides Against Tankyrase Homologue in A549 and HeLa Cells**



**FIG.-9**

**Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC), After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle**

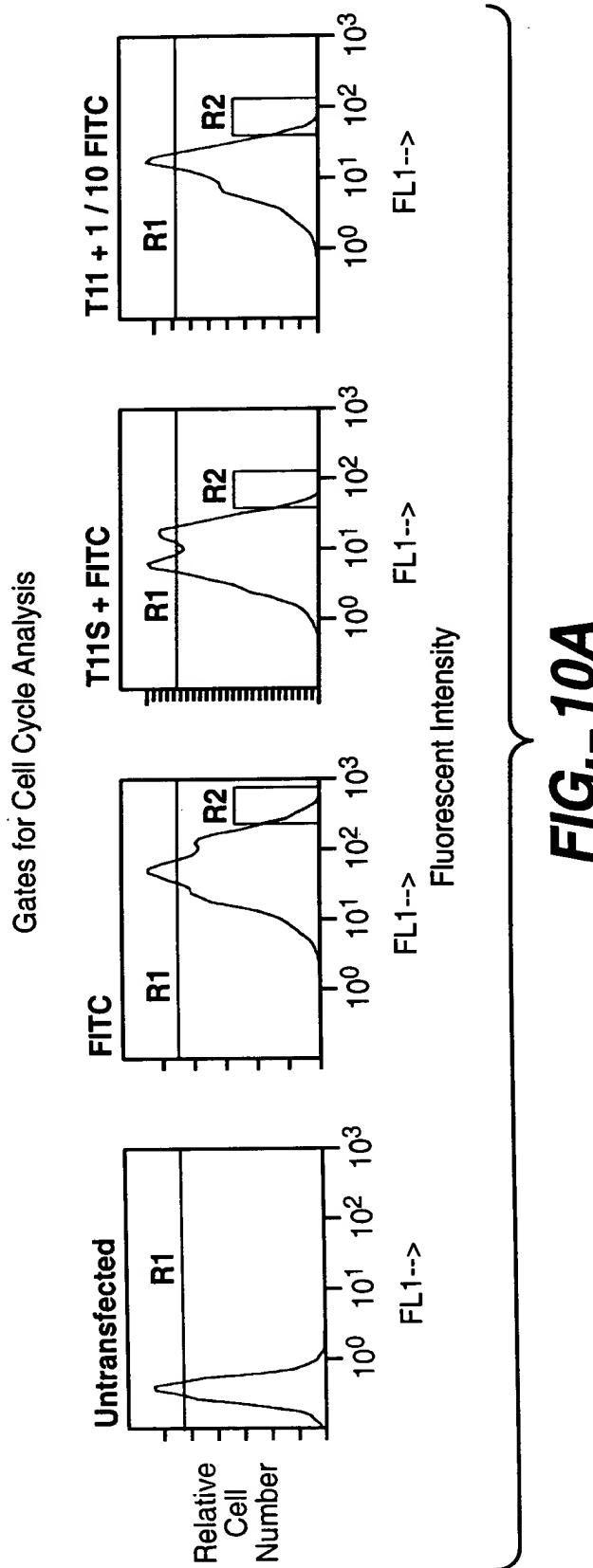
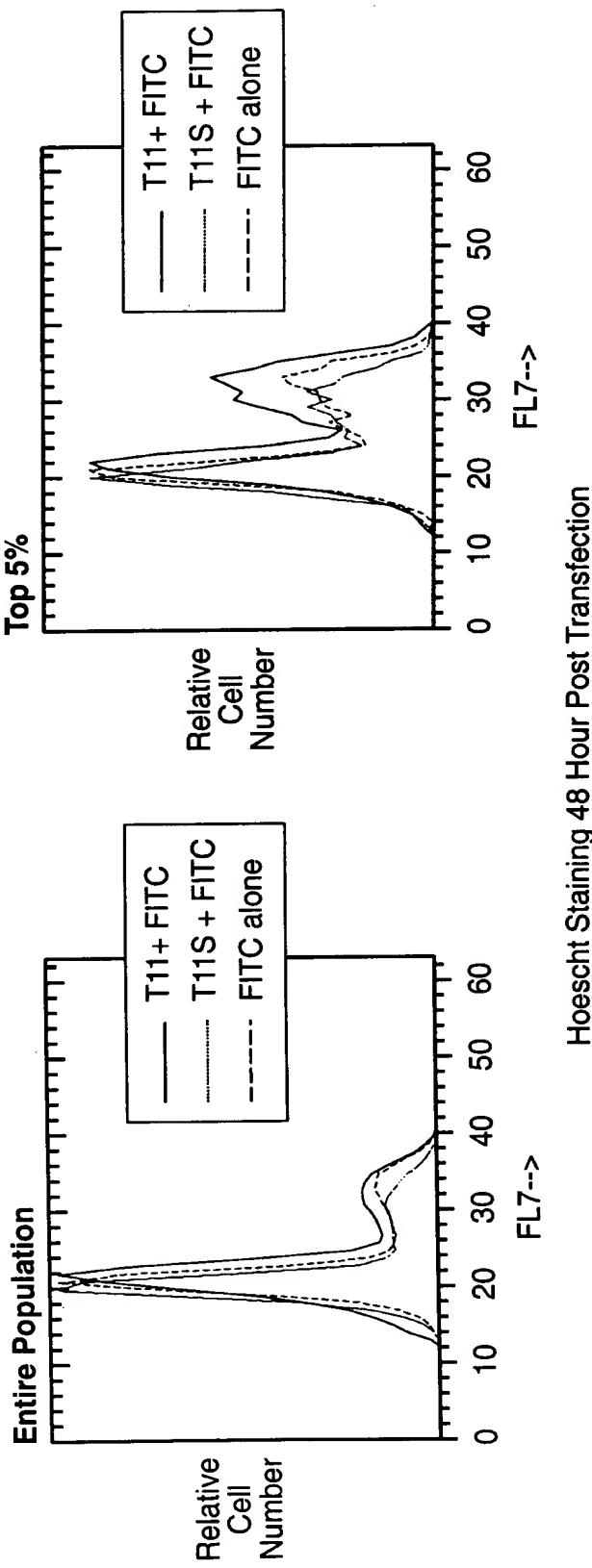


FIG. - 10A

**Cell Cycle Analysis of A549 Cells Transfected with Antisense Oligonucleotides Against Tankyrase Homologue at 48 Hours, Antisense Oligonucleotides (T11) and Control Oligonucleotides (T11S) were transfected with FITC-labeled random 20mer Oligonucleotides (FITC). After 48 Hours, entire population (R1) and Top 5% (R2) of FITC transfected cells were analyzed for cell cycle**

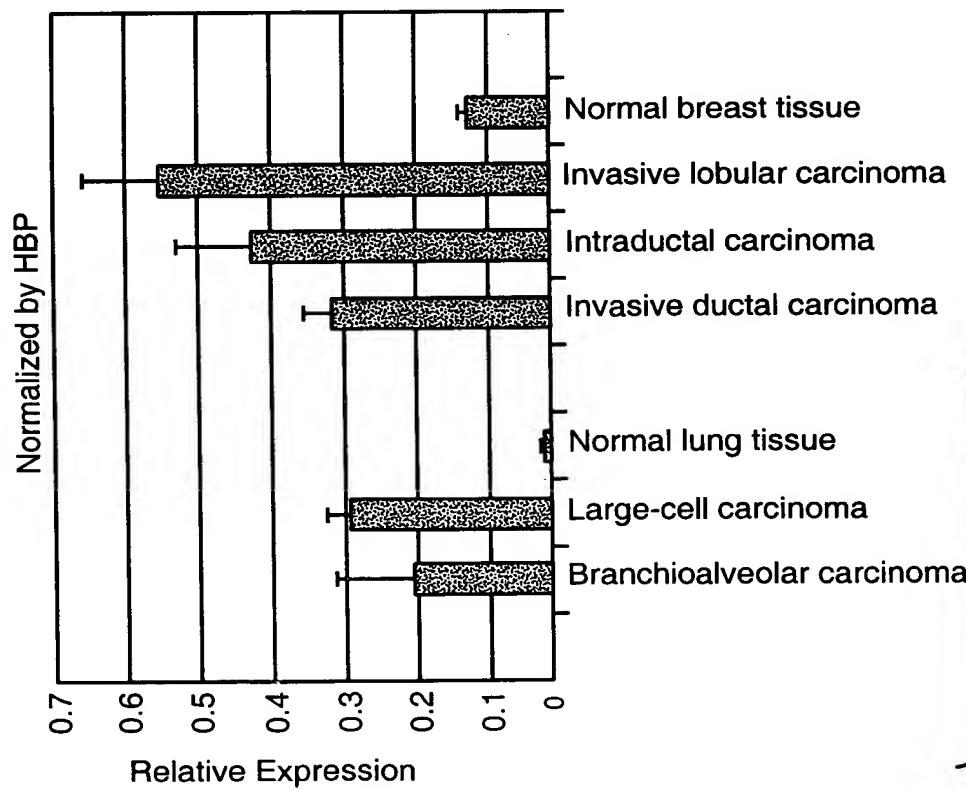
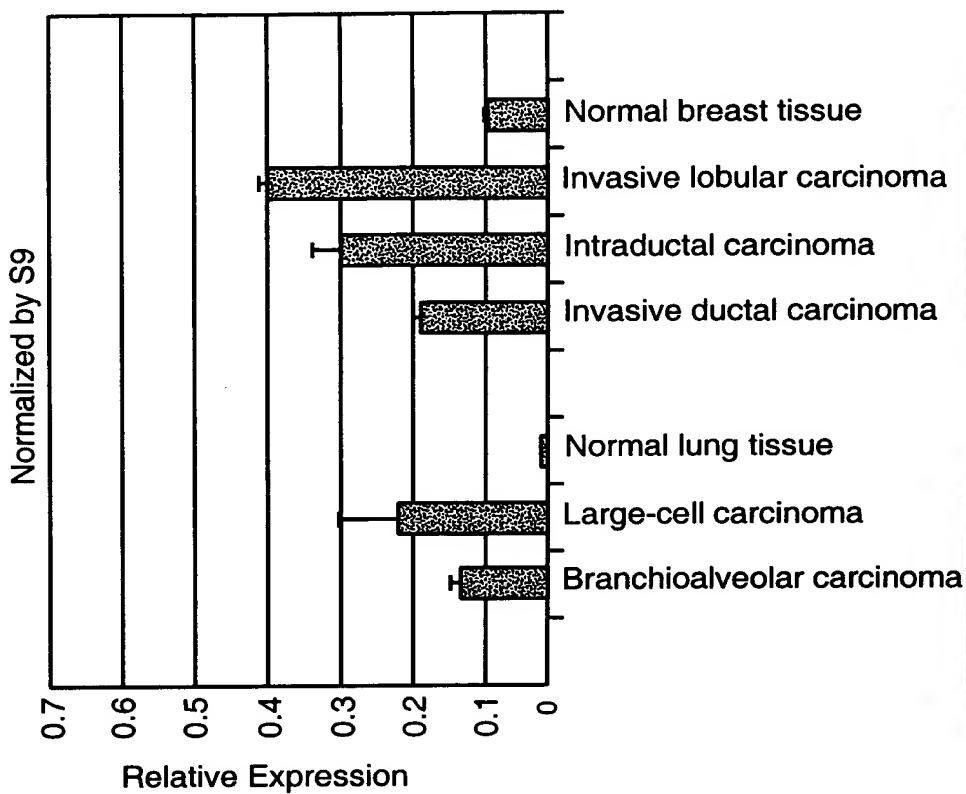
Cell Cycle Analysis



Hoescht Staining 48 Hour Post Transfection

**FIG.\_ 10B**

**mRNA Expression of Tankyrase Homologue in Several Tumors and Normal Tissues by a Taqman Analysis, mRNA Expression was Normalized by 90kDa Highly Basic Protein (HBP) and Ribosomal Protein S9 (S9)**



**FIG.- 11**

Procedure for Nonisotopic Detection of Poly-ADP Ribosylation  
Using Anti-GFP mAb-Coated Plates

Protein lysates from 293T cells normalized by GFP fluorescence and total protein

→

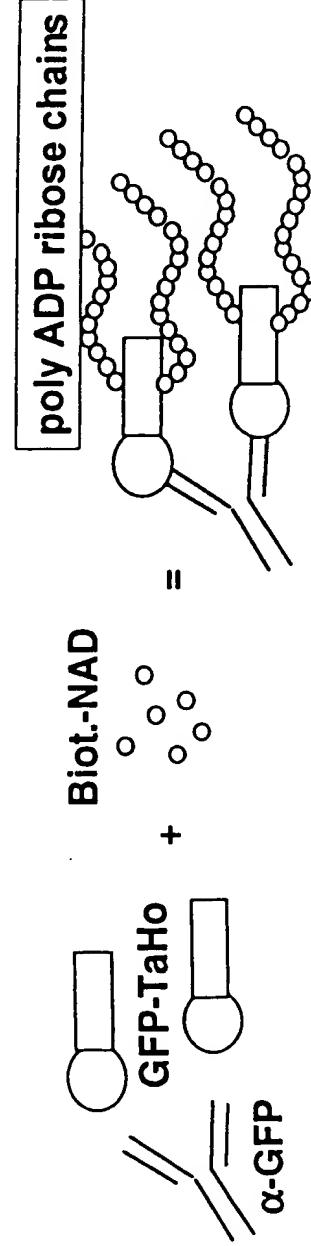
Immobilization of GFP-tankyrase homologue in anti-GFP Coated plates

→

Auto PARR reaction with Biotinylated-NAD in 96 wells

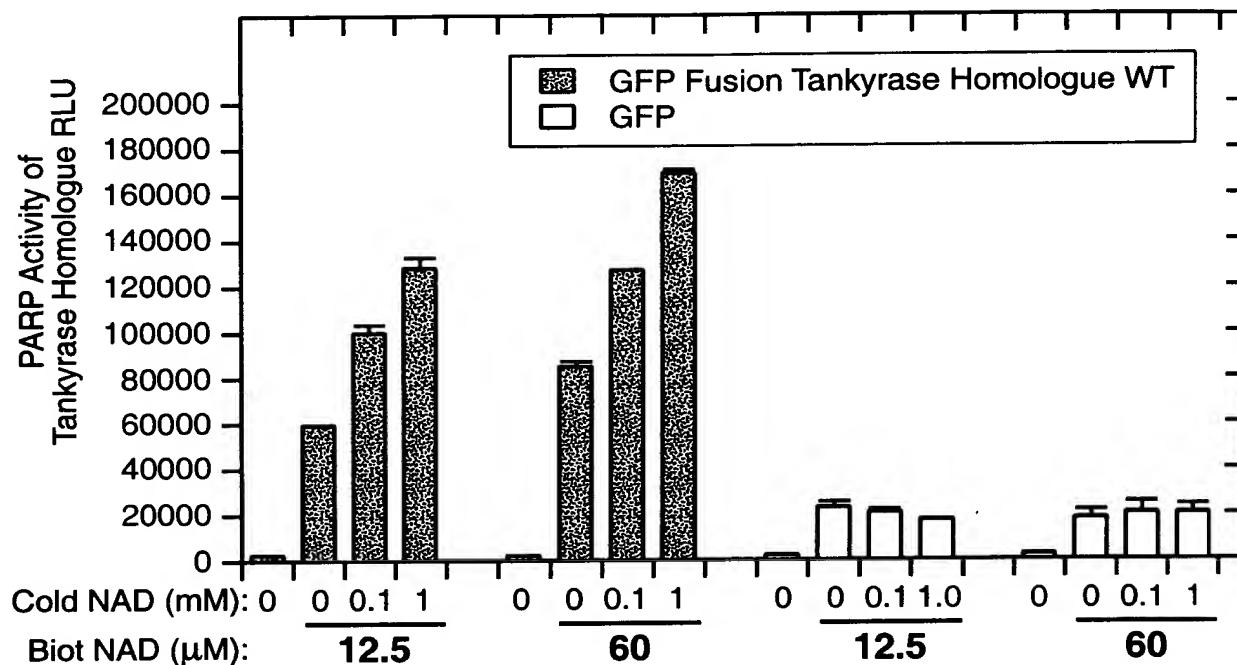
→

Detection of poly ADP ribose chains with Streptavidin-HRP and chemiluminescent substrate



**FIG. 12**

**Non-Isotopic Plate-Based Detection of Taho PARP Activity in the Presence of Biotinylated NAD**



**FIG.\_ 13**

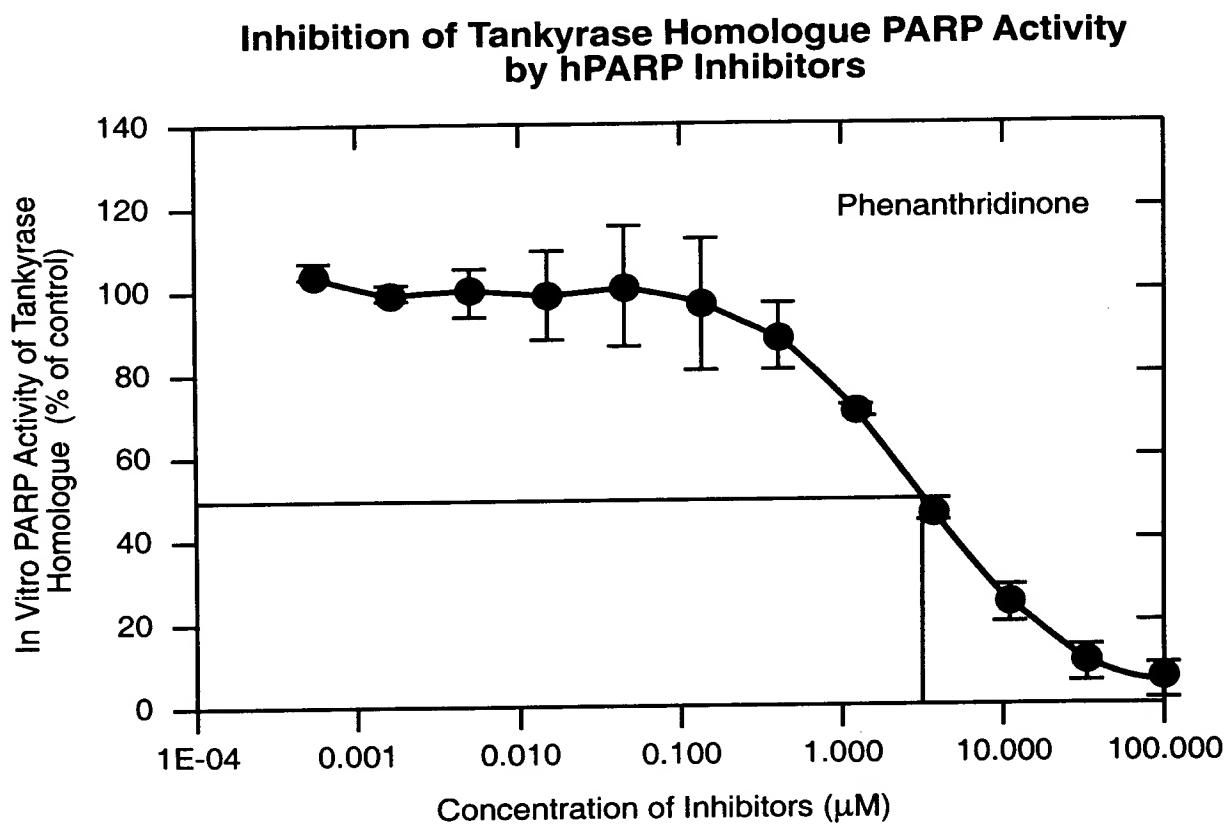
**Comparison of IC<sub>50</sub> Values of the PARP Inhibitors**

	<u>Approximate IC<sub>50</sub> (nM)</u>		<u>hPARP assay IC<sub>50</sub> (nM)</u>		
	<u>TaHo</u>		<u>Rigel</u>	<u>Decker*</u>	<u>Rankin*</u>
3AB	>50 000		5 000	2 000	5 400
6(5H)Phenanthridinone	1 000-2 000		300		
Niacinamide	>50 000		30 000	>>5 000	31 000

\* Decker P et al., Clinical Cancer Research. 1999 May; 5:1169-1172

\* Rawkin PW et al., J Biol Chem. 1989 Mar 15;264(8):4312-4317

**FIG.\_ 14**



**FIG.\_ 15**

**FIG.\_ 16**

**FIG.\_ 16A**

**FIG.\_ 16B**

**FIG.\_ 16C**

**FIG.- 16A**  
**TH-1: Tankyrase Homologue isoform-1, TH-2: Tankyrase Homologue isoform-2**  
**M (Red): the first methionine in the sequence, Z: stop codon**  
**In this figure the first methionine in TH-1 sequence is position 1 (M1)**

Taho C terminus deletion mutant ends at position 429 (K) and adds 28 amino acids because of frame shift.

Tabo E/H mutant has the mutation at position 8/1

Taho E/A dc mutant has the mutation at position 948, ends at position 957 (A) and adds 2 amino acids.

TH-1 AARALASSSPGGLALLLAGPGLLIRLLALLAVAAARIMSGRRCAGGGAACASAAAEEAVE -171  
TH-2

----- \*GFGRKDVVEYLLQNGA -111  
----- PARELFEACRNGDVVERVKRLVTPEKVNNSRDTAGRKSTPLHFAAGFFGRKDVVEYLLQNGA -111  
TH-1  
TH-2

Ankyrin repeat

SVQARDDGGGLIPLHNACSFQHAEVVNILLRHGADPNARDNNWNTPLHEAAIKGKIDVCIV -51  
NVOQARDDGGGLIPLHNACSFQHAEVVNILLRHGADPNARDNNWNTPLHEAAIKGKIDVCIV -51

## Ankyrin repeat

- TH1 start

LLQHGAEPITRNTDGRTALDLADPSAKAVLTGEYKKDELLESARSGNEEKMMLTPLNV 10  
LLQHGAEPITRNTDGRTALDLADPSAKAVLTGEYRRDELLESARSGNEEKMMLTPLNV 10

TH-1  
TH-2

TH-1

## FIG.-16B

	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>
TH-1	NCHASDGRKSTPLHAAAGYNRVKIVQLLIQHGA DVHAKDKGDLVPLHNACSYGHYEVTEL 70	
TH-2	NCHASDGRKSTPLHAAAGYNRVKIVQLLIQHGA DVHAKDKGDLVPLHNACSYGHYEVTEL 70	<u>Ankyrin repeat</u>
TH-1	LVKHGACVNAMD LVQFTPLHEAASKNRVECS LLLISYGADPTLLNCHNKS AIDLAPTPQL 130	
TH-2	LV	<u>Ankyrin repeat</u>
TH-1	KERIAYEFKGHS LQQAAREADVTRIK KHLSSLEMVNFKHP QTHETALHCAA ASPYPKRKQI 190	
	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>
TH-1	CELLRKGAN INEKTEKF LTPLHV ASEKA HNDVV V VV K HEAKV N ALD NLG QTS LHRA AY 250	
	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>
TH-1	CGH IQT C R L L S Y G D P N I I S L Q G F T A L Q M G N E N V Q O L L Q E G I S L G N S E A D R Q L L E A A K A 310	
	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>
TH-1	GD V E T V K K L C T V Q S V N C R D I E G R Q S T P L H F A A G Y N R V S V E Y L L Q H G A D V H A K D K G G L V P 370	
	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>
TH-1	LHNACSYGH Y E A E L L V K H G A V V N V A D L W K F T P L H E A A K G K Y E I C K L L Q H G A D P T K K N 430	
	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>
TH-1	GME I L L W I L K M E I Q I F K I C L G E M Q L C Z RD G N T P L D L V K D G D T D I Q D L L R G D A A L L D A A K K G C L A R V K K I L S S P D V N C R D T Q G R H S T P 490	
	<u>Ankyrin repeat</u>	<u>Ankyrin repeat</u>

**FIG.\_16C**

TH-1	LHLAAGYNNLEVAEYLLQHGA DVAQDKGGGLIPLHNAASYGHVDVAALLIKYNACVNATD	550	
	Ankyrin repeat		Ankyrin repeat
TH-1	KWAFTPLHEAAQKGRTQLCALLAHGADPTLKNQEGQTPLDLVSADDVSALLTAMPSSA	610	
	Ankyrin repeat		Ankyrin repeat
TH-1	LPSCYKPVQVLNGVRSPGATA DALLSSGPSSPSSLSAASSLDNLSGSFSELSVSSSSGTEG	670	
	Ankyrin repeat		Ankyrin repeat
TH-1	ASSLEKKE--VPGVDF SITQFVRNLGLEHLM DIFEREQITLDVLVEMGH KELKEIGINAY	730	
	SAM domain		SAM domain
TH-1	GHRHKLIKGV ERLISGQQGLNPYLT LNTSGSGTILLIDLS PDDKEFQSVEEE MQSTVREHR	790	
TH-1	DGGHAGGIENRYN NILKIQKV CNKWL ERYTHR KEV SEENHN HANER MLFH GSP FVN AII	850	
TH-1	HKGFDERHAY IGGMFGAGIY FAENSSKS NQYYVY GIGGGT GCPV HKDR SCY ICH RQL LFCR	910	
TH-1	• E → L mutation PARP domain		
TH-1	VTLGKSFLQFSAMKMAH SPPGHHSVTGRPS VNGLALA EYYV YRGEQAY PEYLITY QIMRP	970	
TH-1	• E → A • Deletion.		
TH-1	EGMVDG 976		